201-16176A

N-oxydiethylenethiocarbamyl-N'-oxydiethylenesulfenamide (OTOS Accelerator)

CAS No.: 13752-51-7

Rubber and Plastic Additives Panel
American Chemistry Council
January 2006

List of Member Companies in the Rubber and Plastic Additives Panel

The Rubber and Plastic Additives (RAPA) Panel of the American Chemistry Council (ACC) includes the following member companies: Alco Chemical Corporation; Ciba Specialty Chemicals Corporation; Chemtura (formerly Crompton Corporation); Eliokem, Inc.; Flexsys America L.P.; The Goodyear Tire & Rubber Company; The Lubrizol Corporation; and Noveon, Inc. (which is now a subsidiary of the Lubrizol Corporation).

Executive Summary

The RAPA Panel and its member companies hereby submit the final test plan for N-oxydiethylenethiocarbamyl-N'-oxydiethylenesulfenamide (commonly known as OTOS) accelerator to the Environmental Protection Agency's (EPA's) High Production Volume (HPV) Chemical Challenge Program (Program). In a submission dated December 3, 2001, OTOS was included in a category called "Sulfenamide Accelerators." After considering comments received from EPA and the public, on December 18, 2003 the Panel submitted a revised test plan for OTOS as a single chemical rather than as part of a category. The Panel has now completed testing proposed in the revised test plan and hereby submits the final test plan and associated robust summaries to complete the commitment to sponsor OTOS in the HPV Program.

In consideration of animal welfare concerns to minimize the use of animals in the testing of chemicals, the Panel conducted an extensive literature search for all available data, published and unpublished. The Panel also performed an analysis of the adequacy of the existing data.

As described in the report that follows, this sulfenamide accelerator, which has a structure consisting of two morpholine molecules (R_1/R_2) that are attached to a dithiocarboxy group [$R_1SC(S)R_2$], is used as a primary accelerator in natural and synthetic rubbers. Its use in rubber products requires limited water solubility, high organic/oil solubility, relatively low melting point and low vapor pressure. Available data indicates that OTOS is moderately soluble in water, has low potential to bioconcentrate and will not persist in the environment. It is acutely toxic to aquatic organisms and low concern with respect to acute mammalian toxicity. *In vitro* studies have shown that OTOS is mutagenic in a number of assays. It is also carcinogenic at high doses in laboratory rats. A number of studies, including one showing the absence of histopathological findings in reproductive tissues from a long-term feeding study in rats, indicate that OTOS is not a reproductive or developmental toxin.

With the completion of additional testing conducted to supplement the existing data, the Panel now considers the data described below and in the IUCLID robust summary to be adequate for purposes of the

OTOS Accelerator (CAS No. 13752-51-7)

were in the 10 to 100 mg/L range.

Mammalian Toxicology – Acute

Acute mammalian toxicity studies have been conducted with OTOS (Table 1). The data indicate that OTOS has a low order of toxicity (Oral LD_{50} = 5,200 mg/kg).

Mammalian Toxicology – Repeated Dose Toxicity

Repeat dose studies have been conducted with OTOS. A two-year feeding study established a NOAEL of 200 ppm for chronic effects of OTOS in rats. An increased incidence of urothelial tumors was observed in rats at the high dose (600 ppm). This response is consistent with the positive genotoxicity data described below.

Mammalian Toxicology - Mutagenicity

Data from bacterial reverse mutation assays, *in vitro* and *in vivo* chromosome aberration studies, as well as additional supporting *in vitro* and *in vivo* genetic toxicity studies were reviewed. OTOS yields positive results in a number of *in vitro* assays that have been used as screens for carcinogenic potential. These data are consistent with the increased incidence of tumors in the two-year feeding study.

Mammalian Toxicology - Reproductive and Developmental Toxicity

Data from the male fertility, dominant lethal, and two year feeding studies in rats with OTOS were reviewed. The data were determined to be adequate for purposes of the HPV program. Based on the absence of reproductive effects in the male fertility and dominant lethal studies and the absence of any histopathological changes in reproductive organs in the two year feeding study, OTOS was determined to be a low concern for reproductive toxicity.

An oral dietary reproductive/developmental screening study in the rat using OECD Guideline No. 421 was conducted with OTOS. The test material was administered at dietary concentrations of 60, 200 and 600 parts per million (ppm) to groups of ten male and ten female rats throughout maturation, mating, gestation and up to day 4 post partum. In adults, no mortalities or clinical signs of toxicity were observed at 600 ppm or lower concentrations. No macroscopic or microscopic abnormalities were observed at *post mortem* examination. No treatment-related effects were identified on fertility, mating performance, gestation length and subsequent offspring pre or post-natal viability growth or development. In offspring, no treatment-related effects on litter size at birth, litter weight, or subsequent offspring survival throughout lactation were observed. No effects were noted on either offspring reflexological responses or on the intra-litter sex ratios.

Background Information: Manufacturing, Commercial Applications, and Exposure

Manufacturing

OTOS has been manufactured in the USA for approximately 25 years. It is manufactured by reacting morpholine, carbon disulfide and bleach in an aqueous medium. In 1999 Noveon Corporation notified EPA that this chemical was not a high production volume chemical. To the best of the RAPA Panel's understanding, OTOS continues to be produced in the US at levels below the level defined by EPA as a high production volume chemical.

Commercial Applications

The sole known commercial use of OTOS is as a general-purpose vulcanization accelerator for natural and styrene-butadiene rubbers. It is primarily used in the manufacture of tires. Typical usage for OTOS accelerators is from 0.5 to 2 parts accelerator per every 100 parts of rubber (phr).

Shipping/Distribution

OTOS is shipped globally from its manufacturing plant in North America.

Worker/Consumer Exposure

OTOS is only sold to industrial users as ingredients in rubber compounding processes. Available information indicates that there are no direct sales to the general public. Exposure of workers handling OTOS is likely to be greater in the area of material packaging than during chemical manufacturing. When first introduced, the product was manufactured only in a powder form. However, dustless forms are now available which reduce the potential for inhalation exposure. Product forms that minimize dust generation, coupled with the mechanized materials handling systems of the large industrial users, combine to keep exposures to minimum levels. However, during packing operations at the manufacturing site and, to a somewhat lesser degree during weighing activities at the customer site, there may be a potential for skin and inhalation exposure. As noted previously, inhalation exposure is minimized by the dustless forms.

Consumer exposure is minimal. Only very small amounts are used in rubber processing, and the materials themselves become bound in the rubber matrix during the vulcanization process. The most likely route of consumer exposure is skin contact from rubber or latex articles. Skin irritation, or possibly an allergic skin reaction may occur, but only in sensitive individuals subjected to prolonged and repeated exposure, especially under moist conditions.

Summary

The data described above and in the IUCLID robust summary are adequate for purposes of the HPV Chemical Challenge Program. These data indicate that OTOS does not pose a significant hazard to the environment. It hydrolyzes rapidly under acid conditions and is biodegradable (42% after 28 days). It is shown to be not highly toxic to aquatic organisms and is not expected to bioaccumulate. OTOS has however yielded positive results in a number of short-term assays that have been used to screen for possible carcinogens and caused urothelial tumors in rats following long-term dietary administration of 600 ppm OTOS. Cancer risk from dust exposure in the workplace is mitigated by work practices, protective equipment, and engineering controls. OTOS is used in trace quantities and is bound in the rubber matrix during the vulcanization process. While consumer exposure is minimal, skin irritation or possibly skin sensitization may occur in sensitive individuals that have prolonged or repeated contact with the finished rubber article.

Table 1. Test Data Adequacy Assessment for OTOS Accelerator

End Point	Available Data	Assessment
Molecular Weight	248.36	A
Melting Point	130.0° C to 140.0° C; 124.3˚ C (EPI)[1]	A
Boiling Point	353˚ C (EPI)[1]	A
Relative Density	0.6 g/cm3	A
Vapor Pressure	1.53x10(-5)hPa	A
Partition Coef. (logPow)	45.1, $\log_{10} P_{ow}$ 1.65	A
Water Solubility	0.127 g/l @ 20.0 ± 0.5° C	A
Photodegradation	$T_{1/2}$ = 0.6 hr (AOP)[2]	A
Hydrolysis	14.2 min. @ pH 4; 44.4 hrs. @ ph 7; no pseudo-first order kinetics @ ph 9	A
Biodegradability	42% after 28 days; not readily biodegradable	A
Fugacity Level III	Air = <0.01%; Water = 50.2%; Soil = 49.7%; Sediment = 0.0927%	C
Acute Fish Toxicity	8.4 mg/l 96 hr. LC_{50}; NOEC = 2.6 mg/l	A
Acute Invertebrate Toxicity	2.0 mg/l 48 hr. EC_{50}; NOEC = 0.56 mg/l	A
Algal Toxicity	23 mg/l 72 hr. EbC_{50}; ErC_{50} = 51 mg/l; NOEC = 6.25 mg/l	A
Acute Toxicity	Oral LD50 = 5,200 mg/kg bw (rat)	A
Repeated Dose	NOAEL = 200 ppm (2 year feeding study, rats)	A
Mutagenicity:– gene mutation	Ames = negative; *E. coli* = negative; Mouse Lymphoma Assay = positive	A
Mutagenicity – chromosome	CHO chromosomal aberration assay = positive (-act); *E. coli* DNA Damage & Repair = positive; *In vivo* Dominant Lethal Assay (DL) = negative	A
Reproductive Toxicity	No reproductive effects in Male Fertility or DL Assays; No pathology changes in reproductive organs at doses up to 600 ppm in 2 yr rat feeding	A
Developmental Toxicity	NOAEL = 600 ppm (adults and offspring; highest conc. in food)	A

Legend for Table 5: A = Adequate data available
C = Endpoint requirement fulfilled based on calculated data
(-act) = without metabolic activation
CHO = Chinese hamster ovary cells

References

1. EPIWIN modeling Program. Meylan, W. and Howard, P. (1999), Syracuse Research Corporation. Environmental Science Center, 6225 Running Ridge Road, North Syracuse, NY 13212-2510.

2. AOP Program, version 1.89. EPIWIN modeling Program. Meylan, W. and Howard, P. (1999) Syracuse Research Corporation. Environmental Science Center, 6225 Running Ridge Road, North Syracuse, NY 13212-2510.